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#4

Atty Docket 0953.001
PATENT

CERTIFICATION UNDER 37 CFR §1.10

I hereby certify that this New Application and the documents referred to as enclosed herein are being deposited with the United States Postal Service on this date **June 29, 1993** in an envelope bearing "Express Mail Post Office To Addressee" Mailing Label Number **RB637793904** addressed to: Patent Application, Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Ling-Fong Chung — Ling-Fong Chung

29 June 93 — Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Gospodarowicz *et al.*

Serial No. Not Yet Assigned — Group Art Unit: Not Yet Assigned

Filed: June 29, 1993 — Examiner: Not Yet Assigned

For: A TRUNCATED KERATINOCYTE GROWTH FACTOR (KGF) HAVING INCREASED BIOLOGICAL ACTIVITY

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97 (b), Applicants bring to the attention of the Examiner the documents listed on the attached PTO 1449. This

Information Disclosure Statement is being filed within three months of the filing date of the above-referenced application.

Copies of the listed documents are attached. Applicants respectfully request that the Examiner consider the listed documents below and make appropriate notations on the attached PTO 1449 form.

1. Rubin *et al.*, PCT Patent Application, Publication No. WO 90/08771, relates to a substantially pure human keratinocyte growth factor protein or KGF-like protein having an apparent molecular weight of about 25 to 30 kD. Additionally, the publication pertains to a DNA segment encoding the KGF protein and related products.

2. Bellosta, P. *et al.*, J. Cell Biol. 121(3):705-713 (1993), relates to a study of "the role of glycosylation in the secretion of K-FGF," by mutating "human K-*FGF* cDNA to eliminate the glycosylation signal." Expression of the mutated cDNA resulted in "two NH_2-terminally truncated peptides of 13 and 15 kD," the larger of which (K140) was expressed in bacteria and found to have 36 NH_2-terminal amino acids "present in the mature form of K-FGF... deleted. (Abstract)

3. Finch, P.W. *et al.*, Science 2:752-755 (1989), relates to keratinocyte growth factor (KGF) "as a human mitogen that is specific for epithelial cells." The authors found that the "complementary DNA sequence of KGF demonstrates that is a member of the fibroblast growth factor family." (Abstract)

4. Ron, D. *et al.*, J. Biol. Chem. 268(4):2984-2988 (1993), pertains to prokaryotic expression of recombinant KGF (rKGF). The authors found that rKGF "was mitogenic with a specific activity around 10-fold higher than native KGF." The authors generated "a series of KGF mutants with sequential deletions of the amino terminal domain...." The authors found that, among other things, "[b]iological activity of mutants with deletions up to 10 residues was comparable to that of rKGF. However,

deletion of 29 residues resulted in significantly reduced ability to stimulate KGF receptor -kinase activity and DNA synthesis ...." (Abstract)

Remarks

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If it should be determined that any of the listed documents do not constitute "prior art" under United States law, applicants reserve the right to present to the office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of the Statement, please charge the fee to our Deposit Account No. 03-1664.

Respectfully submitted,

Dated: 6/29/93

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